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HEPATOPROTECTORS OR CORRECTOR OF LIVER METABOLIC PROCESSES

Actuality. *In acute and chronic diseases, under the influence of drugs prescribed to treat diseases of vital systems, liver function suffers, which can gradually cause hepatitis, fibrosis, and fatty degeneration. These drugs, as well as pathological conditions, cause:*

1) inhibition of lipid peroxidation;

2) disruption of cell membrane stabilization;

3) increased content of glutamine, taurine and sulfates;

4) increasing the activity of enzymes involved in oxidation and cell function;

5) inhibition of the synthesis of pro-inflammatory cytokines and other inflammatory factors.

6) reduction of hepatocyte necrosis, stimulation of collagenase activity and blockade of connective tissue synthesis enzymes, which causes an antifibrotic effect.

In this regard, it is necessary to continue to study in more detail the mechanisms of action of hepatoprotectors of various origins and determine effective and average doses, and pay attention to the prevention of liver function and metabolism disorders.

***Purpose of the study is** to provide classifications of hepatoprotectors, to reveal their origin and mechanisms of action.*

***Materials and methods.** Based on domestic and foreign literature and online publications SCOPUS, "Web of Science", Google Scholar, determine the mechanism of action and pharmacodynamics of the studied hepatoprotectors.*

***Research results and discussion.** Phytohepatoprotectors are multicomponent metabolic correction systems that increase the adaptive resistance of hepatocytes at the molecular and subcellular levels. The priority mechanism of their action is the antioxidant effect: inhibition of lipid peroxidation and stabilization of the structural and functional state of biomembranes, which ensures the preservation of the phospholipid matrix of cells and the elimination of cytolytic syndrome. Energy support of the liver is realized through stimulation of aerobic ATP synthesis and activation of enzymes of the second phase of xenobiotic biotransformation, which directly increases the detoxification capacity of the organ. The systemic effect is manifested in the regulation of the cytokine profile, limitation of mesenchymal-inflammatory reactions and prevention of fibrous transformation of stellate cells.*

A significant group of hepatoprotectors is made up of phytopreparations. The pharmacological profile of the agents is determined by the biochemical composition of their plant sources:

1. Milk thistle (Silybum marianum) provides molecular repair of membranes by stimulating the biosynthesis of proteins and phospholipids (preparations "Karsyl", "Legalon", "Silibor", "Darsil", "Heparsil").

2. Field artichoke (Cynara scolymus) and turmeric (Curcuma longa) intensify lipid metabolism and choleresis ("Hofitol", "Artibel", "Cynarix", "Holiver").

3. Greater celandine (Chelidonium majus) and common rue (Fumaria officinalis) provide antispasmodic correction of the biliary tract ("Hepabene", "Hepatofalk Planta").

4. Helichrysum arenarium and Schisandra chinensis enhance the secretory function of the liver and induce microsomal enzymes ("Flamin", "Bicyclol", "Tricyclol").

5. Andrographis hairy, dandelion, papaya (Carica papaya), chionanthus and waxwort provide a combination of antitoxic and digestive functions, enhancing systemic adaptation ("Hepophil", "Bonjigar", "Natural Medicines").

Of the synthetic hepatoprotectors, the tripeptide consisting of cysteine, glutamic acid and glycine is quite well known. Synthetic drugs also include the combined drug Hepaglyph and Heparcin. Essential phospholipids Essentiale Forte or Essentiale N are widely prescribed. Lecithin belongs to the group of fatty esters. Lipin is a form of lecithin. Very often in Europe, bile acid preparations are prescribed, especially ursodeoxycholic acid.

In practical medicine, the synthetic drug Antral is often prescribed for hepatoprotection, which protects the metabolism of the liver and pancreas. For self-treatment, as well as on the advice of a doctor, Alohol is recommended, which contains dry bile, dry nettle leaves, and charcoal. Its advantage is the ability to reduce flatulence.

***Conclusions.** The data presented in the article will expand the range of knowledge regarding the classification, pharmacodynamics, and mechanisms of action of hepatoprotectors and will be able to present them as correctors of liver function metabolism in pathological conditions.*

***Key words:** liver, function, hepatoprotectors, correctors of metabolic processes.*

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ГЕПАТОПРОТЕКТОРИ АБО КОРЕКТОРИ ОБМІННИХ ПРОЦЕСІВ ПЕЧІНКИ

Актуальність. *Під час гострих і хронічних захворювань під впливом лікарських препаратів, що призначають для лікування захворювань життєво важливих систем, страждає функція печінки, що поступово може викликати гепатит, фіброз, жирову дистрофію. Такі лікарські засоби, а також патологічні стани зумовлюють:*

1) пригнічення пероксидного окиснення ліпідів;

2) порушення стабілізації мембран клітин;

3) збільшення вмісту глутаміну, таурину та сульфатів;

4) збільшення активності ферментів, що беруть участь в окисненні та функції клітини;

5) пригнічення синтезу прозапальних цитокінів та інших факторів запалення;

6) зменшення некрозу гепатоцитів, стимуляція активності колагеназ і блокада ферментів синтезу сполучної тканини, що зумовлює антифібротичну дію.

У зв'язку з цим необхідно продовжувати більш детально вивчати механізми дії гепатопротекторів різного походження та визначати ефективні і середні дози, звертати увагу на профілактику порушень функції та метаболізму печінки.

Мета дослідження *– навести класифікації гепатопротекторів, розкрити їх походження та механізми дії.*

Матеріали та методи. *На підставі вітчизняної, зарубіжної літератури й інтернет-видань SCOPUS, "Web of Science", Google Scholar визначити механізм дії та фармакодинаміку досліджуваних гепатопротекторів.*

Результати дослідження та їх обговорення. *Фітогепатопротектори є мультикомпонентними системами метаболічної корекції, які підвищують адаптаційну стійкість гепатоцитів на молекулярному та субклітинному рівнях. Пріоритетним механізмом їхньої дії є антиоксидантний ефект: інгібування пероксидного окиснення ліпідів та стабілізація структурно-функціонального стану біомембран, що забезпечує збереження фосфоліпідного матриксу клітин і ліквідацію цитолітичного синдрому. Енергетична підтримка печінки реалізується через стимуляцію аеробного синтезу АТФ та активацію ферментів другої фази біотрансформації ксенобіотиків, що прямо підвищує детоксикаційну спроможність органу. Системний вплив проявляється у регуляції цитокінового профілю, обмеженні мезенхімально-запальних реакцій та запобіганні фіброзній трансформації зірчастих клітин.*

Значну групу гепатопротекторів становлять фітопрепарати. Фармакологічний профіль засобів зумовлений біохімічним складом їхніх рослинних джерел:

1. Розторопша плямиста (Silybum marianum) забезпечує молекулярну репарацію мембран через стимуляцію біосинтезу білків і фосфоліпідів (препарати «Карсил», «Легалон», «Силібор», «Дарсіл», «Гепарсил»).

2. Артишок польовий (Cynara scolymus) та куркума висока (Curcuma longa) інтенсифікують ліпідний обмін та холерез («Хофітол», «Артібель», «Цинарикс», «Холівер»).

3. Чистотіл великий (Chelidonium majus) та рутка лікарська (Fumaria officinalis) здійснюють спазмолітичну корекцію жовчовивідних шляхів («Гепабене», «Гепатофальк планта»).

4. Безсмертник пісковий (Helichrysum arenarium) та лимонник китайський (Schisandra chinensis) посилюють секреторну функцію печінки та індукують мікросомальні ферменти («Фламін», «Біциклол», «Трициклол»).

5. Андрографіс волосистий, кульбаба лікарська, папая (Carica papaya), хіонантус та восковиця забезпечують поєднання антитоксичної та травної функцій, підвищуючи системну адаптацію («Гепофіл», «Бонджигар», «Природні ліки»).

Із синтетичних гепатопротекторів досить відомим є трипептид, який складається з цистеїну, кислоти глутамінової та гліцину. До синтетичних лікарських засобів належить також комбінований препарат гепагліф та гепарцин. Широко призначають препарати есенціальних фосфоліпідів – есенціале форте або есенціале Н. Лецитинін належить до групи жироподібних ефірів. Ліпін є формою лецитину. Дуже часто у Європі призначають препарати жовчних кислот, особливо урсодезоксихолеву кислоту.

У практичній медицині часто призначають з метою гепатопротекції синтетичний препарат антраль, який захищає обмін печінки та підшлункової залози. Для самостійного лікування, а також за порадою лікаря рекомендують алохол, який містить суху жовч, сухе листя кропиви, вугілля. Його перевагою є здатність зменшувати метеоризм.

***Висновки.** Наведені у статті дані розширять коло знань щодо класифікації, фармакодинаміки і механізмів дії гепатопротекторів, а також зможуть представити їх як коректори обміну функції печінки у разі патологічних станів.*

***Ключові слова:** печінка, функція, гепатопротектори, коректори обмінних процесів.*

Introduction. Relevance. In clinical practice, individual acute and chronic liver diseases are rarely diagnosed. More often they occur as complications of diseases of the nervous, cardiovascular, digestive, and urinary systems. In all industrialized countries, there is an increase in liver diseases. A special place in the treatment of liver pathology is occupied by drugs belonging to the group of hepatoprotectors. These are compounds of various origins, the action of which is aimed at restoring homeostasis in hepatocytes.

The use of such agents helps to increase the organ's resistance to the effects of pathogenic factors, normalize functional activity and stimulate reparative and regenerative processes in the liver. Due to these effects, hepatoprotectors are used for liver diseases, pathologies of internal organs complicated by organ damage, as well as as a means of medical cover when prescribing drugs with hepatotoxic effects. Almost all hepatoprotectors have an anti-inflammatory effect, contribute to increasing antioxidant activity.

Research objective – to provide classifications of hepatoprotectors, to reveal their pharmacodynamics and mechanisms of action.

Research methods. Based on domestic and foreign literature and online publications SCOPUS, "Web of Science", Google Scholar, determine the mechanism of action and pharmacodynamics of the studied hepatoprotectors.

Research results and their discussion. To date, there is no single classification of hepatoprotectors. This group of drugs includes more than 700 drugs, including individual chemical compounds, combined and herbal drugs containing combinations of plant, animal, amino acid and vitamin components. Most often, they are distinguished depending on the origin, composition and mechanism of action. (Bilovol & Kniazkova, 2019).

The classification of hepatoprotectors by origin includes:

1) Herbal preparations:

a) preparations of natural or semi-synthetic milk thistle flavonoids;

b) licorice (glycyrrhizic acid) preparations;

c) preparations of natural or semi-synthetic flavonoids from other plants;

2) Animal products;

3) Essential phospholipid preparations;

4) Detoxifying drugs (are not classic hepatoprotectors, but are able to reduce the toxic effects associated with hepatocellular insufficiency by reducing the formation or increasing the utilization of endogenous toxicants):

a) drugs with direct detoxifying effect;

b) drugs with indirect detoxifying effects (reduce the formation of endogenous toxins, activate the formation of metabolites or accelerate the metabolism of toxins)

5) Bile acid preparations;

6) Drugs of different groups.

By the nature of their effect on pathological processes in the liver, drugs are divided into the following groups:

1). Means that affect the manifestations of cytolysis syndrome and reduce fatty infiltration of the liver. Aimed at restoring the integrity of cell membranes and normalizing fat metabolism (essentiale forte).

2). Drugs that affect the manifestations of cholestasis syndrome. This group includes ursodeoxycholic acid preparations (ursofalk, ursosan) and compounds containing S-adenosylmethionine (heptral).

3). Detoxifying agents. Used for acute and chronic alcohol intoxication (metadoxil, ropren), as well as for toxic liver damage. These include drugs containing flavonoids from various plants.

4). Drugs that prevent the development of fibrosis. Recommended for use in the stage of liver cirrhosis. Includes ursodeoxycholic acid preparations, polyprenol groups, milk thistle flavonoids, and Laennec.

5). Agents with antiviral activity. This category includes drugs containing milk thistle flavonoids and agents that stimulate interferon synthesis.

6). Agents that stimulate hepatocyte regeneration and immunomodulatory drugs. Aimed at restoring cellular structure and activating immune defense.

7). Drugs with combined hepato- and neurotropic action. They have a combined effect on the functional state of the liver and indicators of the central and peripheral nervous system.

According to the modern classification (Radchenko et al., 2021), it was proposed to divide hepatotropic agents by frequency of use, multiplicity of mechanisms of action, and effectiveness into preparations of plant origin, amino acid complexes and essential phospholipids, bile acid derivatives, and other animal, synthetic, and combined agents.

One of the most widely used is the classification that summarizes and systematizes data on the clinical use of drugs for which hepatotropic action is dominant or has independent clinical significance, and which includes the following groups:

1. Herbal preparations:

1.1. Milk thistle preparations.

1.2. Preparations of other plants.

2. Preparations of animal origin.

3. Preparations containing essential phospholipids (EPL) and preparations of semi-unsaturated fatty acids.

4. Drugs with a predominantly detoxifying effect:

4.1. Direct-acting drugs.

4.2. Indirect acting drugs:

4.2.1. Drugs that reduce the formation of endogenous toxicants.

4.2.2. Drugs that activate the formation of endogenous detoxifiers.

4.2.3. Drugs that accelerate metabolism
toxicants.

5. Drugs of different groups (Pogotova et al., 2015).

Almost all of these products contain polyphenols and flavonoids, therefore they have a pronounced hepatoprotective effect in tumors (Costea et al., 2022).

Herbal preparations have membrane-stabilizing, detoxifying, antioxidant, antifibrotic and reparative effects. They are prescribed for toxic liver damage, chronic alcoholic hepatitis and cirrhosis. When administered intravenously, it has an antiviral effect in viral hepatitis C.

Milk thistle (Silybum marianum) has been used to treat liver diseases and poisoning since ancient times. The plant contains flavolignans (silymarin), alkaloids, saponins, silychristin, vegetable oil, proteins, histamine, tyramine, vitamin K and other macro- and microelements. The highest concentration of silymarin is in the fruits.

The active ingredients of milk thistle exert a complex pharmacological effect on the hepatobiliary system through a number of interrelated mechanisms. The antioxidant activity of the compounds is due to the ability of phenolic structures to directly bind free radicals (“scavenger” effect), inhibition of cAMP-dependent phosphodiesterase and stimulation of endogenous protective systems, which effectively stops the lipid peroxidation cascade. The membrane-stabilizing and antihepatotoxic effect is based on the activation of RNA polymerase I, intensification of the biosynthesis of structural proteins and phospholipids, as well as on the limitation of the functional activity of transport proteins. This restores the physiological permeability of cell and mitochondrial membranes and prevents the metabolic activation of xenobiotics.

Anti-inflammatory and desensitizing potential is due to inhibition of lipoxygenase, prostaglandin synthase and nuclear factor NF-κB, which reduces the synthesis of leukotrienes (B4) and prostaglandins, stabilizes mast cell membranes and reduces the activity of Kupffer macrophages. The reparative and regenerative effect is provided by intensification of the synthesis of ribosomal RNA and DNA-dependent polymerase I. Antifibrotic properties are manifested through modulation of protein kinases and inhibition of the transformation of stellate cells into myofibroblasts with direct suppression of collagen formation. Additionally, oncoprotective properties have been established through the regulation of apoptosis and cell cycle control. The lack of interaction with the cytochrome P-450 system provides a high safety profile and minimal risk of undesirable effects on the metabolism of other drugs (Radchenko et al., 2021).

Milk thistle preparations are divided into monopreparations (“Legalon”, “Silymar”, “Karsyl”, “Rosilymar”) and combined dosage forms (“Gepabene”, “Bienosilym”, “Sibektan”, “Fosfonciale”, “Gepafor”). A separate group consists of multicomponent systems with a complex nutrient profile, an example of which is “Livonorm”. Each capsule of this product contains a balanced complex: milk thistle extract, antioxidants, α-lipoic acid, N-acetylcysteine, selenium and zinc (Costea et al., 2022).

The pharmacodynamics of these drugs is due to the activity of the flavonoid silymarin – a mixture of three key isomers: silibinin, silicristin and silidianin. Silibinin is determined as the leading component, which determines the main clinical effect. Its anti-inflammatory effect is realized through the blockade of TNF-α-dependent factors and inhibition of the nuclear factor NFκB, which limits the biosynthesis of inflammatory mediators and

caspases. Additionally, silibinin inhibits the activity of phosphodiesterase, slowing down the breakdown of cAMP. This leads to a decrease in the concentration of intracellular calcium in hepatocytes and levels the Ca^{2+}-dependent activation of phospholipases, preventing the destruction of membranes (Pogotova et al., 2015).

The antioxidant potential of silibinin is due to its specific phenolic structure, which allows it to inactivate highly reactive oxygen species and interrupt the lipid peroxidation (LPO) cascade, increasing the liver's resistance to oxidative stress. The metabolitotropic effect of the compound consists in the selective stimulation of RNA polymerase I in the cell nucleus, which activates transcription and synthesis of structural proteins. Importantly, this effect does not extend to altered cells, which eliminates the risk of tumor proliferation.

In experimental and clinical toxicology, the ability of silibinin to block transport systems for grebe toxins (α-amanitin) has been proven, which significantly reduces mortality in acute xenobiotic poisoning. The use of silymarin in viral hepatitis A contributes to the rapid regression of cytolysis phenomena (reduction in ALT and AST levels) and bilirubinemia, reducing the duration of hospitalization. In alcoholic cirrhosis, long-term use of the drug (from 6 months) significantly reduces the activity of transaminases and markers of fibrosis in the blood serum.

In addition to hepatoprotection, the neuroprotective effect of silibinin (through activation of heme oxygenase and protection of neuronal DNA) has been established, as well as its ability to pharmacologically precondition the myocardium, brain, and kidneys, which protects the organs from ischemic-reperfusion injury.

Milk thistle extracts are effectively integrated into combination regimens with other phytocomponents. An example is the drug "Sibektan", where the combination of milk thistle with tansy, birch and St. John's wort provides complex hepatotropic, choleretic and antispasmodic effects, which is pathogenetically justified in chronic lesions of the hepatobiliary system (Aghemo et al., 2022).

When administered intravenously, silibinin is able to block specific binding sites and transport systems of α-amanitin (an inhibitor of RNA polymerase I), one of the leading toxins of the grebe. This mechanism, according to the results of controlled and uncontrolled studies, allows to significantly minimize mortality in patients with xenobiotic intoxication.

Indications for the use of silymarin are liver pathologies with verified clinical and biochemical signs of process activity. A number of small randomized controlled trials have demonstrated the ability of silymarin in viral hepatitis A to promptly stop cytolysis phenomena (according to ALT and AST levels), reduce bilirubin content and reduce the duration of hospitalization compared to placebo. There is also data on the effectiveness of silymarin in chronic forms of viral hepatitis (Omar et al., 2022).

The therapeutic activity of silymarin in alcoholic cirrhosis of the liver has been studied in several clinical studies. Taking the drug for 0.5–3.5 years contributed to a decrease in the levels of transaminases and serum markers of parenchymal fibrosis in alcoholic genesis of lesions. The neuroprotective effect of silibinin was studied in an experiment on models of diabetes mellitus: it was found that the compound provides protection of neuronal DNA and reduces the manifestations of oxidative stress in the brain through the activation of heme oxygenase. When modeling ischemic myocardial damage, it was found that silymarin is able to protect the heart, brain, liver and kidneys from ischemia/reperfusion as a result of preconditioning, although the mechanism of cardioprotection in ischemia remains not fully understood (Sabarathinam, 2024).

Milk thistle extracts are integrated into the composition of combined drugs, which usually contain plant extracts with a choleretic effect. Thus, "Sibektan" (a composition of milk thistle, tansy, birch and St. John's wort extracts) exhibits hepatotropic, choleretic, antispasmodic and anti-inflammatory effects and is used mainly for chronic liver damage. Similar properties are possessed by the drug "Gepabene", consisting of milk thistle and ruta vulgaris extracts. "Bienosilim", in addition to silymarin, contains a complex of ethyl esters of polyunsaturated fatty acids obtained from the micellar fungus Entomophthora virulenta. The drug is indicated for chronic hepatitis, cirrhosis and alcoholic liver damage (Aghemo et al., 2022).

A new approach to the use of milk thistle products was the creation of a silibinin-phospholipid complex with vitamin E (SPM complex). Studies have shown that in patients with fatty liver disease, this drug reduces the level of transaminases, GGTP and alkaline phosphatase, and also suppresses serum levels of IFN-γ, TNF-α and IL-6. The multicomponent drug "Livonorm" is prescribed in phytotherapy regimens for neoplastic processes in metastatic liver disease. Also pathogenetically justified is the use of the Ayurvedic drug "Liv-52", the active ingredients of which are caper bark, chicory seeds, black nightshade, western cassia, terminalia arjuna bark, tamarisk, yarrow seeds, iron oxide) (Priya et al., 2025).

Artichoke leaf extract ("Artihol") realizes its hepatoprotective potential due to the content of phenolic acids (caffeic and chlorogenic), flavonoids

and sesquiterpene lactone. These components exhibit pronounced antioxidant activity, which determines the effectiveness of "Artihol" in liver pathologies associated with the intensification of lipid peroxidation (LPO) – in viral lesions, as well as intoxications with hepatotropic factors, including alcohol. Regeneration of oxidoreductase activity provides support for cellular respiration processes and reduces the severity of peroxide processes (Nasef et al., 2022).

The phytoextract modulates the functional state of hepatocytes, induces enzyme synthesis and enhances the detoxification capacity of the liver. In terms of the strength of the hepatoprotective effect, this agent is comparable to silymarin.

The choleretic effect of the drug is due to the presence of cynarin, which stimulates bile production, increases bile fluidity and activates biliary tract motility. Also, hypolipidemic, hypoazotemic and diuretic properties have been described for artichoke leaf extract. Due to its effect on inducible NO synthesis, artichoke exhibits a coronary dilating effect (Kam et al., 2025).

A representative of complex remedies based on artichoke is "Detoxyl". It contains extracts of artichoke, grapefruit and dandelion. The components of "Detoxyl", in addition to hepatoprotective action, are characterized by neuroprotective and cardioprotective properties. The drug is prescribed for liver diseases, especially in combination with kidney and urinary tract pathology, for non-alcoholic fatty liver disease, and is effective for toxicosis and liver pathology in pregnant women.

The composition of the drug "Liv-52" includes medicinal plants traditionally used in Ayurvedic medicine, in particular: caper bark, wild chicory seeds, black nightshade, western cassia, terminalia arjuna bark, tamarisk, yarrow seeds, as well as iron oxide. Available data confirm the ability of the drug to provide protection of the liver parenchyma from the effects of toxic agents, which is realized through the induction of cytochrome P-450 and acetaldehyde dehydrogenase. The antioxidant effectiveness of the drug is due to an increase in the level of endogenous tocopherols. In addition, "Liv-52" normalizes the activity of Na+/K+-ATPase. (Xu et al., 2022)

Analysis of the clinical use of "Liv-52" in patients with various forms of liver and hepatobiliary tract pathology indicates the therapeutic efficacy of the drug in biliary motor dyskinesia, acute and chronic hepatitis, as well as liver cirrhosis (Kantharia et al., 2023).

The list of other products containing phytocomponents includes "Dipana" and "Bonjigar". These drugs contain complexes of biologically active plant extracts with hepatotropic, choleretic, and antispasmodic action vectors (Sroor et al., 2022).

Pumpkin seed oil ("Tykveol") is a complex of polyunsaturated and unsaturated fatty acids, essential phospholipids, tocopherols, carotenoids, sterols, phytosterols and essential oils. The hepatoprotective effect of tykveol is provided by its membrane-stabilizing properties and is manifested in slowing down the development of damage to hepatocyte membranes and accelerating their recovery.

It has been noted that pumpkin seed oil preparations reduce inflammation, slow down the development of connective tissue and accelerate the regeneration of the damaged liver parenchyma. The drug has a choleretic effect, normalizes the chemical composition of bile, reduces the risk of developing gallstone disease; it is prescribed for chronic forms of liver damage of various etiologies (hepatitis, cirrhosis), as well as for cholecystocholangitis and biliary dyskinesia (Abd-Elhakim et al., 2025).

The drug "Ropren", obtained from pine needles, contains a concentrate of polyprenols. Due to its effect on the synthesis of dolichols (participating in the biosynthesis of glycoproteins), cholesterol, and coenzyme Q, its hepatoprotective activity has been established in the conditions of isoniazid use.

The group of drugs of animal origin is represented by the products "Layennec", "Hepatosan", "Enterosan", "Progepar", "Erbisol".

"Layennec" is a purified hydrolysate of human placenta. Biologically active substances contained in the hydrolysate stimulate the proliferation of hepatocytes, have a detoxifying effect, reduce lipid and cholesterol deposits in liver cells, increase the activity of tissue respiration, activate metabolic processes in the liver, reduce the intensity of connective tissue development in the liver. Its reparative activity is due to the presence of amino acids, low-molecular metabolites and fragments of growth factors. The drug is indicated for non-alcoholic fatty liver disease (NAFLD) and toxic lesions of the organ parenchyma.

Erbisol Ultrafarm contains low-molecular-weight biologically active organic compounds (glycopeptides, peptides, nucleotides, amino acids) obtained from embryonic animal tissue, which activate the body's natural regulatory systems responsible for detecting and eliminating pathological changes and maintaining homeostasis.

"Erbisol Ultrafarm" directs the immune system toward accelerated restoration of damaged cells and the destruction of abnormal cells and tissues. The main immunomodulatory effect is manifested primarily through its action on NK cells (CD3−/16+56+) and T killers (CD3+/16+56+), which are responsible for the elimination of damaged and virus-infected cells that

are incapable of regeneration, as well as abnormal cells (mutant, malignant, virus-carrying cells) and tissues, and through the macrophage component, which is responsible for the repair of damaged cells and the restoration of functional activity of organs and tissues.

At the same time, Erbisol Ultrafarm has an immunocorrective effect and, in cases of immune system disorders, promotes its normalization through activation of T lymphocytes, Th1 helpers, and T killers, which is important for restoring the balance between cellular and humoral immunity in oncological diseases and for terminating allergic processes.

Depending on the immune status of the body, Erbisol UltrafarmH also corrects the activity of certain other factors of humoral and cellular immunity: it induces the synthesis of α-, β-, and γ-interferons (which contribute to viral elimination), tumor necrosis factor, interleukin-2 (IL-2) and IL-12, and suppresses the synthesis of IL-10.

At the same time, Erbisol Ultrafarm activates regenerative processes in the liver, promotes the replacement of dead hepatocytes with functionally complete ones, and has an anti-inflammatory effect.

Erbisol Ultrafarm enhances the effects of antibiotics and exogenous interferons while simultaneously reducing their side effects. Erbisol Ultrafarm is non-toxic, does not accumulate, and has no allergenic, teratogenic, mutagenic, or carcinogenic effects.

Indications: diseases of viral etiology – acute and chronic viral hepatitis B, chronic viral hepatitis C; acute and chronic forms of diseases caused by herpesviruses: Herpes Simplex type I (labial), Herpes Simplex type II (genital), Herpes zoster (shingles); diseases of bacterial etiology – chronic nonspecific lung diseases during periods of exacerbation and remission.

"Hepatosan"– isolated hepatocytes of animal origin, obtained by freeze-drying. The therapeutic effect is based on detoxification by sorption of toxic metabolites in the intestine and partial regeneration of the functional activity of liver cells. The pathogenetic significance in the mechanism of action of "Hepatosan" is the utilization of degradation products of exogenous hepatocytes to restore the structural integrity of the patient's liver. The drug limits the manifestations of cytolysis, stimulates protein synthesis function and has a detoxifying effect in cirrhosis of the liver, aggravated by hepatocellular insufficiency.

"Enterosan" contains a lyophilized substrate of the mucous membrane of the stomach of birds. The mechanism of action is due to the influence of regulatory peptides on the motor function of the gastrointestinal tract and the activation of redox processes under the influence of glycosaminoglycans.

Drug **"Erbisol"** includes a complex of low-molecular biologically active peptides that activate the body's natural defense systems and have an immunostimulating effect. It is prescribed for the treatment of acute and chronic hepatitis of various etiologies.

Syrepar is a hydrolysate of bovine liver extract with a standardized content of cyanocobalamin (vitamin B12) – 10.0 μg/mL. The composition of the drug includes amino acids, low-molecular-weight metabolites and, presumably, fragments of liver growth factors, which determine its reparative properties. Syrepar accelerates regeneration of the liver parenchymal tissue due to its lipotropic effect. It enhances the detoxification properties of hepatocytes. Indications: chronic and subacute hepatitis, liver cirrhosis, fatty liver dystrophy, toxic and drug-induced liver damage.

Phospholipids are the main component of the lipid layer of any cell, including hepatocytes. They participate in the processes of molecular transport, differentiation and division of cells, stimulate the activity of various enzyme systems. Their mechanism of action is associated with the restoration of the content of phospholipids in the cell wall, reducing cytolysis, increasing collagenase activity, and influencing lipid peroxidation.

Essential phospholipids have low bioavailability when administered enterally, since phospholipids in the composition of chylomicrons do not enter the liver, but the lymphatic system, from where they are transported, accumulated and metabolized in adipose tissue. When administered parenterally, they can accumulate in other organs and systems. Prescribed for liver diseases, pathologies of internal organs complicated by liver damage, when prescribing hepatotoxic drugs (Tang et al., 2023).

Monopreparations of essential phospholipids are "Essentiale N", "Essentiale Forte N", "Rezalyut Pro". Combined dosage forms include "Phosphogliv", "Essliver", "Phosfonciale", "Livolin Forte", "Eslidin". A separate group consists of preparations of polyunsaturated fatty acids (Omega-3 triglycerides): "Epadol-neo", "Doppelherz Active Omega-3", "Omakor", "Eikonol", "Sikod" and fish oil.

The EFL substance is a highly purified soybean extract, the key component of which is 1,2-dilinoleoyl-phosphatidylcholine (PC) with a high content of polyunsaturated fatty acids. The hepatotropic effect of EFL is realized through the direct integration of their molecules into the destructively altered phospholipid structures of hepatocyte membranes, which provides an anticytolytic effect. Unsaturated fatty acids in the composition of phospholipids optimize the functional parameters and fluidity of membranes, reduce the density of the phospholipid matrix and normalize permeability

indicators. Exogenous administration of EFL induces the activity of membrane-bound phospholipid-dependent enzymes and transport proteins, which has a supportive effect on the intracellular metabolism of hepatocytes, increasing the detoxification and excretory potential of the organ. The mechanism of action of EFL may also be associated with the inhibition of lipoperoxidation (LPO). However, the antioxidant resource of EFLs is not absolute, since they themselves can act as substrates for peroxidation processes (Chen et al., 2025).

In clinical practice, EFL is used in three vectors: treatment of liver diseases and its toxic intoxications; therapy of pathologies of internal organs accompanied by secondary liver damage; pharmacological protection when using hepatotoxic drugs. It should be noted that intensive parenteral therapy with EFL drugs in conditions of active hepatitis requires verified caution, in particular in patients with severe cholestasis syndrome (Rajappa et al., 2024).

Phospholip ("Universal Medicare", India) is a complex of essential phospholipids. One capsule contains: lecithin (equivalent to 175 mg of phospholipids – phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, and phosphatidylserine) 350 mg, soybean oil 200 mg. The active substances of the drug are essential phospholipids – phosphatidylcholine, phosphatidylethanolamine, phosphatidylinositol, phosphatidylserine, and linoleic acid, which are contained in soybean lecithin. Essential phospholipids are found in the membranes of cells and cellular organelles of almost all tissues of the body, as well as in erythrocyte membranes. In striated skeletal muscles, kidneys, and lungs, they are present in smaller amounts. The half-life of Phospholip is 30 hours. After oral administration, Phospholip is hydrolyzed by 90% by the pancreatic enzyme phospholipase A2 in the gastrointestinal tract, and only 50% of the hydrolyzed Phospholip is absorbed in the intestine. Phospholip normalizes protein and fat metabolism and has a lipotropic effect. The essential phospholipids contained in the drug are components of liver cell membranes and are necessary for the formation, stabilization of structure, and regeneration of hepatocyte membranes. Phospholipids improve membrane function, including ion exchange, tissue respiration, biological oxidation, regulate the binding of intracellular respiration enzymes in mitochondria, as well as oxidative phosphorylation in cellular energy metabolism. Phospholip restores impaired immune functions of lymphocytes and macrophages caused by alcohol and viruses. It increases the detoxification function of the liver, improves the emulsifying properties of bile, and prevents the formation of gallstones. Indications for use: acute and chronic hepatitis, fatty degeneration of the liver, liver cirrhosis, food and drug poisoning, toxic and radiation-induced liver damage; atherosclerosis; gestosis.

Essentiale ("Rhone-Poulenc Rorer", USA/France; "Natterman", Germany) is a combined drug that contains highly purified essential phospholipids – diglyceride esters of choline phosphoric acid and unsaturated fatty acids from soybean extract (linoleic acid – approximately 70%, linolenic acid, and others). In addition, Essentiale contains vitamins (riboflavin, thiamine, pyridoxine, cyanocobalamin, tocopherol, nicotinamide, pantothenic acid). In liver diseases, the drug provides the supply of readily assimilable high-energy essential phospholipids that penetrate liver cells and are incorporated into their membranes. Essential phospholipids normalize liver function and enzymatic activity of hepatocytes, reduce the level of energy expenditure of the liver, and promote hepatocyte regeneration. Indications for use: chronic hepatitis, liver cirrhosis, fatty dystrophy, toxic liver damage (tetracycline, rifampicin, paracetamol, etc.); radiation syndrome; pregnancy toxicosis; prevention of recurrence of gallstone disease; normalization of lipid metabolism in patients with coronary heart disease; psoriasis; radiation syndrome.

Livolin Forte contains, in addition to the main active ingredient phosphatidylcholine, vitamins B1, B2, B6, B12, tocopherol, and nicotinamide. Livolin Forte enriches the membranes of cells and cellular organelles of hepatocytes with phosphatidylcholine, restores their integrity, activates membrane enzymes, stimulates prostaglandin synthesis, and increases the synthetic function of the liver, i.e., the ability to synthesize vital proteins (albumin, prothrombin, blood coagulation factors). Livolin regulates lipid and lipoprotein metabolism in the liver, stabilizes bile composition, eliminates cholestasis and cytolysis, and prevents the development of fibrolosis and liver cirrhosis. An important effect of Livolin Forte is its ability to increase the detoxification capacity of hepatocytes, usually reduced in hepatitis and liver cirrhosis. The components of Livolin Forte effectively influence various pathogenetic links in liver damage. B-group vitamins included in the drug are cofactors of enzymes involved in biochemical processes and thus protect hepatocyte membranes. Thus, vitamins B1 and B2 enhance redox processes, eliminate hypoxia, and improve oxidative phosphorylation in mitochondria. Vitamins B6 and B12 actively stimulate biosynthetic processes in hepatocytes.

Tocopherol is a structural component of cell membranes and exhibits pronounced antioxidant

properties, preventing damage to cellular structures by free radicals. It also participates in tissue respiration, heme biosynthesis (the structural basis of hemoglobin and other proteins), fat and carbohydrate metabolism, and other metabolic processes. Indications for use: acute and chronic hepatitis (alcoholic, drug-induced, radiation, viral etiology), fatty liver dystrophy; radiation syndrome; psoriasis. Phospholipids are incorporated into the structure of cell membranes and regulate the activity of phospholipid-dependent enzyme systems of the liver (see Essentiale N).

Flakumin (a sum of flavonol aglycones from smoketree leaves) has pronounced antioxidant and choleretic effects. It promotes bile secretion from the gallbladder by eliminating spasm of the bile ducts. The vitamins included in the drug act as cofactors in biochemical processes. The drug promotes hepatocyte regeneration, improves microcirculation in the liver, and has a hypolipidemic effect. Indications for use: acute (during the convalescence period) and chronic hepatitis, fatty liver degeneration of various etiologies, alcoholic and drug-induced liver damage, liver cirrhosis, poisoning, gestosis of pregnancy, psoriasis. A similar pharmacological profile is characteristic of **Essel-Forte**, which contains essential phospholipids and a vitamin complex.

The active substances of **Livolact** are essential phospholipids (see Essentiale N) and lactulose. In liver diseases, essential phospholipids restore the structure of hepatocyte membranes, regenerate damaged mitochondria, increase impaired enzyme system activity, and thus normalize function and enhance the detoxification role of the liver.

Lactulose is a disaccharide that is not absorbed in the gastrointestinal tract. In the large intestine, under the influence of intestinal microflora, it is converted into low-molecular organic acids (lactic, acetic). As a result, pH decreases, osmotic pressure in the intestine increases, which stimulates peristalsis and leads to evacuation of fecal masses.

In liver failure, lactulose binds ammonia and other toxic protein breakdown products, promoting their excretion with feces, and also reduces their formation in the large intestine due to decreased pH and inhibition of proteolytic bacteria growth. When pH decreases, free ammonia is converted into ionized ammonia, which is poorly absorbed and excreted with feces. Indications for use: chronic hepatitis, cirrhosis, liver failure, prevention of gallstone formation.

Phosphogliv contains phosphatidylcholine from soybeans and trisodium salt of glycyrrhizic acid. Phosphatidylcholine included in the drug reduces inflammation, hepatocyte necrosis, their fatty infiltration, and clinical manifestations of liver diseases. At present, there has been evident progress in the development, study, and implementation of this class of drugs into clinical practice, not only abroad but also in Ukraine. Convincing evidence of this is the appearance on the domestic pharmacological market of such agents as Phospholip, Essel-Forte, Lipin, as well as clinical trials of new drugs Lipofen, Lioliv, and Eplir.

Lipin, a parenteral preparation (lecithin preparation), is a lyophilized egg phosphatidylcholine in liposomal form. Pharmacokinetic studies of phosphatidylcholine liposomes have established their high hepatospecificity. Up to 97% of phosphatidylcholine administered in liposomal form is detected in hepatocytes, which explains the high effectiveness of the drug. Lipin does not exert a negative effect on the functional state of organs and body systems, is non-toxic, and does not accumulate in the body. Lipin has hepatoprotective, cardioprotective, anti-inflammatory, antihypoxic, antioxidant, and detoxifying effects. Lipin exhibits a membrane-protective effect, increases nonspecific immunity, and improves microcirculation and rheological properties of blood. In various models of liver damage in animals, it has been shown that the drug stabilizes hepatocyte membranes, increases the number of T and B lymphocytes, improves metabolic processes (increases glycogen and nucleic acid content), and external secretory activity of the liver. Lipin also promotes surfactant synthesis in the lungs. The drug is a white or light-yellow powder with a characteristic odor. It is easily suspended in aqueous solutions with the formation of liposomes (liposomal emulsion). Indications for use: acute and chronic active hepatitis, chronic non-calculous cholecystitis, liver cirrhosis, nonspecific ulcerative colitis; late gestosis.

Lioliv. Due to the complex of metals introduced into the structure of liposomes, the presence of antioxidant effects, and the membrane-regenerating action of liposomes, Lioliv exhibits hepatoprotective properties, in particular, activates protein-synthetic processes and improves bile-forming and bile-excreting functions of the liver. Under the influence of the drug, biochemical indicators of liver function tests improve, clinical manifestations of the disease decrease, the general condition of patients improves, and the level of adaptation increases. According to the results of preclinical studies, it was established that Lioliv, when administered parenterally and enterally in acute, subacute, or chronic toxic liver damage, weakens the effect of hepatotoxins, activates reparative processes in hepatocytes, and contributes to normalization of the structural and functional state of the liver in experimental animals of

various species. The hepatoprotective effect is due to inhibition of lipid peroxidation processes, maintenance of endogenous antioxidant systems, stabilization of liver structure and hepatocyte membranes, activation of reparative reactions in the liver and adaptation level, as well as nonspecific detoxification function.

Lioliv provides a high protective effect and can compete with traditional hepatoprotective agents (Essentiale, Silibor) in the treatment and prevention of hepatopathy due to its complex effect on various pathogenetic links of toxic hepatitis (membrane lipid peroxidation, cholestasis, cytolysis, inflammatory process). In clinical practice, Lioliv is intended for corrective therapy of acute and chronic dystrophic and inflammatory liver lesions (toxic, alcoholic, drug-induced hepatitis; fatty steatosis) and liver cirrhosis.

Eplir is a fraction of polar lipids from lake silt sediment (sulfide mud). The biological activity of Eplir is determined by the presence of phospho- and sulfolipids, α-, β-, and γ-carotenes, xanthophylls, chlorophyll and its derivatives, prostaglandins, sterols, myxoxanthophylls, as well as high-molecular-weight acids.

Eplir has pronounced antioxidant properties, as a result of which it inhibits non-enzymatic lipid peroxidation processes and accumulation of toxic peroxidation products that damage hepatocytes. It also enhances antioxidant defense in the body: due to the presence of thiol compounds, it promotes glutathione synthesis – the central link of the antioxidant system's anti-radical chain. In models of toxic hepatitis and ethanol-induced hepatosis, hepatoprotective activity of Eplir has been demonstrated. In experiments, it prevents the development of exudative and proliferative components of inflammation in the liver, reduces the number of necrotized hepatocytes, stabilizes membranes of lysosomes, endoplasmic reticulum, mitochondria, and cytolemma of parenchymal cells.

As an inhibitor of free radical reactions, it reduces the formation of toxic lipid peroxidation products (diene conjugates, Schiff bases, malondialdehyde), increases the antiradical activity of membrane lipids, and potentiates the function of endogenous antioxidants – vitamin E and reduced glutathione. In addition, Eplir stimulates the excretory function of hepatocytes; increases cytochrome P-450 activity, as well as conjugation enzymes – glutathione S-transferase, which catalyzes conjugation of xenobiotics with reduced glutathione, and bilirubin glucuronyl transferase. According to experimental data, Eplir surpasses the known foreign drugs Essentiale and Legalon in hepatoprotective activity and contributes to maintaining high levels of phosphatidylcholine and phosphatidylethanolamine in hepatocyte membranes.

Clinical studies of Eplir indicate improvement in the general well-being of patients with impaired liver function against the background of chronic persistent hepatitis or fatty hepatosis; reduction or disappearance of pain syndrome and dyspeptic symptoms. In most patients, a reduction in liver size up to complete normalization was noted, absence or reduction of jaundice or icterus of the skin and sclera, normalization of initially elevated transaminase and alkaline phosphatase activity, decrease in bilirubin and γ-globulin levels in blood serum.

Method of use (shake the vial before use): burns, frostbite, injuries, sprains, purulent wounds, panaritium, furuncles, carbuncles, stomatitis, herpes – apply tampons, wipes, or drainage soaked in Eplir solution to the affected area once daily; inflammation of the ear, throat, nose – instill 2–3 drops 3 times daily until complete recovery; conjunctivitis, blepharitis, eye injuries and burns – instill 1–2 drops 3 times daily for up to 7 days; hemorrhoids – apply sterile tampons soaked in oily Eplir solution after defecation for 2 weeks; diseases of the musculoskeletal system – perform massage or manual therapy using oily Eplir solution; prostate adenoma and prostatitis — insert sterile oil-soaked tampons rectally; colpitis – insert sterile tampons soaked in Eplir intravaginally; pressure sores, trophic ulcers – apply sterile oil-soaked wipes to the affected area; radiation therapy – apply to the mucosa immediately after irradiation several times daily.

Metadoxyl (metadoxine) has detoxification, hepatoprotective and anti-alcohol effects. The mechanisms of activity of the drug are based on the stimulation of alcohol dehydrogenase and antioxidant effects – as a precursor of glutathione – in combination with effects at the level of the central nervous system. The latter include the effect on the cholinergic system, an increase in dopamine content and a decrease in glutamate levels. The hepatoprotective activity of metadoxine is due to the membrane-stabilizing effect and the ability to restore the balance of saturated and unsaturated free fatty acids. This increases the resistance of hepatocytes to lipid peroxidation processes that occur under the influence of toxic factors (Kvanchakhadze et al., 2025).

The detoxification potential of the drug is realized through the activation of liver enzymes that ensure the metabolism of ethanol – alcohol dehydrogenase and acetaldehyde dehydrogenase. This mechanism accelerates the elimination of ethanol and acetaldehyde from the body, minimizing their toxic effects. Metadoxine prevents the accumulation of triglycerides in hepatocytes, and also inhibits the synthesis of fibronectin and collagen – this slows down the development of cirrhotic changes. The drug reduces mental and somatic manifestations of hangover syndrome, shortening

the duration of abstinence. At the level of the central nervous system, the drug activates the cholinergic and GABA-ergic systems, improves cognitive functions and memory, prevents motor excitement caused by ethanol. Metadoxine also has a nonspecific antidepressant effect and reduces the craving for alcohol. It is prescribed mainly for alcoholic liver damage, chemotherapy, acute or chronic alcohol intoxication (Jiang et al., 2022).

Ursodeoxycholic acid (UDCA) is a hydrophilic, non-toxic tertiary bile acid that is the 7β-epimer of chenodeoxycholic acid. The mechanisms of action of UDCA are complex and remain the subject of active study. The drug has complex hepatoprotective properties – anticholestatic, choleretic, antioxidant, antiapoptotic, antifibrotic and immunomodulatory effects. UDCA displaces hydrophobic bile acids, which leads to a decrease in the lithogenicity of bile and a decrease in the toxic effect on hepatocytes. Due to the effect on farnesoid X receptors, which are responsible for the transport of bile acids, it ensures their removal (efflux) from liver cells. The antioxidant effect of UDCA consists in reducing oxidative stress and restoring the structure of intracellular organelles. This prevents the release of hydrolases into the cytosol and cell destruction. By normalizing the permeability of mitochondrial membranes, UDCA reduces the release of cytochrome C and inhibits the activity of caspases - this stops the mechanisms of premature death (apoptosis) of liver cells. The immunomodulatory effect of UDCA is associated with a decrease in the expression of HLA class I and II molecules on the surface of hepatocytes and cholangiocytes. The antifibrotic effect is realized through a decrease in the number of fibrogenesis activators and direct inhibition of the activity of hepatic stellate cells. UDCA is also able to affect lipid and carbohydrate metabolism. This occurs through interaction with nuclear receptors (TGR5 and farnesoid X receptor-alpha) and stimulation of the synthesis of glucagon-like peptide-1 (Milivojac et al., 2024; Teslenko et al., 2024).

The main indications for the use of UDCA include primary biliary cirrhosis, primary sclerosing cholangitis, as well as chronic hepatitis with signs of cholestasis (including alcoholic and drug-induced). The drug is used in the treatment of cystic fibrosis, intrahepatic biliary atresia, and cholestasis that occurs after transplantation or against the background of parenteral nutrition. A separate group of indications is intrahepatic cholestasis in pregnant women. UDCA is also prescribed for chronic viral hepatitis - as an independent agent when antiviral therapy is not possible or as part of a combination treatment. In addition, the drug is effective in non-alcoholic steatohepatitis (Teslenko et al., 2024).

Thioctic (alpha-lipoic) acid, D, L-α-5-(1,2-dithiolan-3-yl) valeric acid (Berlition, Thiogamma, Thioctacid, Thioctic acid, Espa-Lipon, Biletan, Tioctan) is found in various organs of the body; large amounts are present in the liver, kidneys, and heart. It is an endogenous antioxidant that ensures the binding of free radicals. Thioctic (alpha-lipoic) acid is an endogenous antioxidant that provides binding of free radicals. In the body, the compound is formed during oxidative decarboxylation of alpha-keto acids (Belenichev et al., 2019). By the nature of its biochemical action, it is close to B-group vitamins. Lipoic acid exhibits antioxidant activity, participates in the regulation of lipid and carbohydrate metabolism, shows a lipotropic effect, and affects cholesterol metabolism (Belenichev et al., 2024). As a coenzyme of mitochondrial enzyme complexes, it participates in the metabolism of pyruvic acid and other alpha-keto acids. The drug helps to reduce blood glucose levels, glycogen accumulation in the liver and reduce insulin resistance. Thioctic acid regulates lipid and carbohydrate metabolism, affects cholesterol levels and improves the functional state of the liver. The drug has a detoxifying effect in poisoning with heavy metal salts and other intoxications. The following effects are characteristic of the drug – hepatoprotective, hypolipidemic, hypocholesterolemic and hypoglycemic. Thioctic acid also improves the nutrition (trophy) of neurons (Superti & Russo, 2024). Thioctic (alpha-lipoic) acid acts as a coenzyme in the processes of oxidative decarboxylation of pyruvic acid and alpha-keto acids. It plays a significant role in the bioenergetics of liver cells by regulating carbohydrate, protein, and lipid metabolism, and also exhibits pronounced lipotropic and antioxidant properties. Lipoic acid improves liver function, exerts hepatoprotective and detoxifying effects, and is effective in intoxications (with barbiturates, alcohol, heavy metal salts, and mushroom poisoning). According to experimental data, lipoic acid has an immunomodulatory effect and exhibits antioxidant activity. Indications for use are diabetic and alcoholic polyneuropathy.

Lipamide (an amide of lipoic acid) structurally replaces the hydroxyl group with an NH_2 group. The indications for its use are the same as those for lipoic acid; however, lipamide is better tolerated and causes adverse effects less frequently. In therapeutic doses, hepatoprotectors are safe agents. Very rarely, diarrhea is observed when using high doses of essential phospholipids. The use of UDCA may be accompanied by temporary weakening of bowel movements, and the use of ademetionine – by unpleasant sensations in the epigastric region. In some cases, allergic reactions occur in the form of skin itching and rashes. In patients with

bronchial asthma, bronchospasm may develop when a metadoxine solution is administered. Contraindications to the appointment of agents are hypersensitivity to their components, as well as periods of pregnancy and lactation. For ornithine preparations, renal failure is an additional limitation (Najafi et al., 2022).

According to experimental and clinical studies, phospholipid preparations improve the histological picture of the liver in chronic hepatitis – they limit the manifestations of fibrosis, cytolysis and cholestasis. The effectiveness of EFL depends on the use of high doses and sufficient duration of treatment courses. An example of a combined agent is the drug "Phosphogliv", which contains phospholipids and glycyrrhizinic acid. The oral form of this combination acts primarily as a phospholipid agent due to the low bioavailability of glycyrrhizinate, while the parenteral form works primarily due to the latter (Milivojac et al., 2024).

Glycyrrhizinic acid has an immunostimulating effect – it activates phagocytosis, increases the activity of natural killer (NK) cells and stimulates the production of interferon-gamma. In addition, it has antiviral effects, antioxidant properties and affects nuclear factor kv and tumor necrosis factor. It has been established that glycyrrhizinic acid changes the structure of the surface antigen of the hepatitis B virus, which leads to its retention in the Golgi apparatus (Bi et al., 2023).

The hepatoprotective effect of omega-3 unsaturated fatty acid preparations has also been confirmed. They act as lipid metabolism modulators, antioxidants, and cell membrane stabilizers. These compounds also exhibit pronounced cardioprotective properties.

Direct-acting drugs include compounds based on ornithine-aspartate and glutamine-arginine. The main function of these drugs is to reduce toxemia that occurs in hepatocellular insufficiency of various origins. This occurs through the direct interaction of the components with internal toxins – primarily ammonia (Sales et al., 2024).

L-ornithine-L-aspartate contains two amino acids that actively participate in the biochemical cycles of the liver. Ornithine stimulates the first enzyme of the urea cycle and acts as a substrate for the creation of citrulline. Aspartate is integrated into the cycle at the stage of arginine succinate synthesis, and also serves as the basis for the production of glutamine. The latter process ensures the binding of ammonia in liver cells, brain tissues and other organs. The drug is prescribed for fatty dystrophy, hepatitis and cirrhosis, accompanied by hyperammonemia, as well as for the correction of brain disorders on the background of liver dysfunction. The group of drugs that reduce the formation of endogenous toxins includes lactulose and lactitol. Lactulose is a disaccharide consisting of galactose and fructose. The human body does not have the necessary enzymes for its breakdown, so the substance passes through the gastrointestinal tract unchanged (Abd El Salam & Abd Elrazik, 2024).

In hepatic encephalopathy, the therapeutic effect of the drug is provided by inhibiting the synthesis of ammonia by bacteria and inhibiting the breakdown of amino acids and urea. Lactulose helps reduce the level of ammonia in the ileum – this occurs by inhibiting the activity of the enzyme glutaminase or by directly binding toxic compounds.

Lactitol works on a similar principle. In the colon, under the influence of microflora, it is converted into low-molecular organic acids. This lowers the pH and stimulates the transfer of ammonia from the blood to the intestine in the form of ammonium ions, which are not absorbed and are excreted from the body. Thus, the drugs reduce the toxic load on the nervous system and improve the clinical condition of patients with liver failure (Gubergrits et al., 2025).

The group of drugs that activate the formation of endogenous detoxifiers includes ademetionine and remaxol. These drugs reduce the symptoms of toxemia in hepatocellular insufficiency by stimulating the synthesis of metabolites that provide the body's cleansing function.

Ademethionine (S-adenosine-L-methionine) is a coenzyme of natural origin that participates in methyl group transfer reactions. In transmethylation reactions, it ensures the biosynthesis of phospholipids, and in transsulfation processes, the synthesis and turnover of glutathione and taurine. This contributes to the binding and excretion of bile acids and xenobiotics. Ademethionine also participates in aminopropylation, which is necessary for the synthesis of polyamines – putrescine, spermidine and spermine. These compounds are important for the formation of the structure of ribosomes and cell repair processes.

Under the influence of the drug, the expression of the MAT1A gene, which is responsible for the synthesis of the enzyme methionine adenosyltransferase, is enhanced. This enzyme is necessary for the processing of methionine, which enters the body with food. Not only ademetionine itself is important for the implementation of hepatotropic effects, but also its metabolic product – methylthioadenosine. In addition to the effect on the liver, the drug exhibits anti-neurotoxic and antidepressant effects. The therapeutic effect is manifested at the end of the first week of administration and stabilizes within two weeks of treatment.

Ademetionine belongs to the group of hepatoprotectors with concomitant antidepressant activity. The drug exhibits

choleretic, cholekinetic, detoxification, regenerative, antioxidant and neuroprotective effects. The agent fills the deficiency of endogenous S-adenosyl-L-methionine, stimulating its synthesis in the body. The highest concentrations of the compound are observed in the tissues of the liver and brain. Ademetionine plays a fundamental role in metabolism, participating in key biochemical processes: transmethylation (the compound is a methyl group donor for the synthesis of membrane phospholipids, neurotransmitters, nucleic acids and proteins) and transsulfation (ademetionine is a precursor of cysteine, taurine and glutathione (which provides a mechanism of cellular detoxification), as well as an acetylation coenzyme that supports the energy potential of the hepatocyte). The drug increases the content of glutamine in the liver, cysteine and taurine in the blood plasma. By decarboxylation, ademetionine participates in aminopropylation reactions as a precursor of polyamines – putrescine (a stimulator of hepatocyte regeneration), spermidine and spermine, which are part of the structure of ribosomes, which reduces the risk of fibrotization (Pogotova et al., 2015).

The choleretic effect of ademetionine is due to the normalization of the synthesis of its own phosphatidylcholine, which increases the mobility and polarization of membranes. This improves the function of bile acid transport systems and promotes their passage into the biliary tract. The drug demonstrates effectiveness in intrapartum cholestasis.

Ademetionine reduces the toxicity of bile acids in the hepatocyte by binding them to taurine or sulfates. Sulfation of bile acids facilitates their elimination by the kidneys and excretion with bile. In addition, sulfated forms additionally protect liver membranes from the effects of toxic non-sulfated bile acids. In patients with diffuse liver diseases (cirrhosis, hepatitis), ademetionine reduces the severity of skin itching and improves biochemical indicators: direct bilirubin concentration, alkaline phosphatase and aminotransferase activity. The therapeutic effect persists for up to 3 months after discontinuation of treatment. The drug has been proven effective in hepatopathies caused by the action of various toxic agents (Kukharchuk et al., 2025).

Indications for the use of ademetionine are intrahepatic cholestasis in precirrhotic and cirrhotic conditions that develop with fatty liver disease, chronic hepatitis, and toxic parenchymal lesions of various etiologies. In particular, the drug is effective in intoxications of alcoholic, viral, and drug genesis induced by prolonged use of antibiotics, antitumor, antituberculosis, antiviral agents, tricyclic antidepressants, and oral contraceptives.

The use of ademetionine is justified in the complex therapy of chronic acalculous cholecystitis, cholangitis and cirrhosis of the liver. A separate group is the treatment of encephalopathies, including those associated with liver failure (in particular, alcoholic genesis). The drug is also indicated for the correction of intrahepatic cholestasis in pregnant women. In addition to the hepatotropic effect, ademetionine is used to reduce symptoms of depression and increased fatigue that accompany chronic liver diseases (Bhamare et al., 2025).

Betaine citrate, an analogue of a natural metabolite formed during the oxidation of choline, has an effect similar to ademetionine. Betaine participates in the transmethylation reaction of homocysteine, contributing to the formation of methionine. The latter is the basis for the synthesis of S-adenosylmethionine, a universal source of methyl groups necessary for the biosynthesis of phospholipids. In addition, betaine can act as a direct donor of methyl groups for the methylation of phosphatidylethanolamine. In non-alcoholic fatty liver disease, the drug improves biochemical parameters, but does not affect the histological picture even with prolonged use (Seo et al., 2023).

Remaxol is an original drug that combines the properties of a balanced polyionic solution and a hepatotropic agent. It contains methionine, inosine, nicotinamide and succinic acid. Methionine is actively involved in the synthesis of choline, lecithin and other phospholipids, and with the participation of methionine adenosyltransferase, it contributes to the formation of endogenous ademetionine.

Thanks to inosine, the total pool of purine nucleotides necessary for the resynthesis of macroergs (ATP and GTP), secondary messengers and nucleic acids increases. Inosine is also able to inhibit the activity of xanthine oxidase, which reduces the production of reactive oxygen species. Succinic acid provides antihypoxic action by supporting the succinate oxidase link and exhibits an indirect antioxidant effect, preserving reserves of reduced glutathione. Nicotinamide activates NAD-dependent enzyme systems. These processes support the energy supply of hepatocytes and activate synthetic processes in them. In addition, succinic acid can affect Ito cells through specific receptors, acting as a paracrine agent.

It has been experimentally proven that Remaxol reduces liver damage by toxic agents, reduces the severity of dystrophic changes and activates regeneration. Clinical studies have confirmed its significant effect on the manifestations of toxemia, cytolysis and cholestasis. The drug is effective in viral hepatitis, drug-induced and alcoholic liver damage. In non-alcoholic steatohepatitis, it can be used as a means of starting therapy. Similar to ademetionine, Remaxol has an antidepressant and

antiasthenic effect. In acute alcohol intoxication, the drug reduces the incidence of delirium and shortens the duration of hospital stay, slightly surpassing ademetionine in effectiveness (Maksymenko et al., 2025).

The group of drugs that accelerate the metabolism of toxins includes benzobarbital, phenobarbital and metadoxine. These drugs do not directly interact with toxic compounds, but stimulate the activity of hepatic systems responsible for the processing of endogenous and exogenous substances. Their use is advisable in chronic intrahepatic cholestasis, functional hyperbilirubinemia on the background of diffuse liver diseases – in particular, Gilbert's syndrome – and in the treatment of neonatal jaundice.

Previously, flumecinol, phenobarbital, and benzobarbital were used to accelerate bilirubin metabolism. The therapeutic effect of these agents is based on the induction of cytochrome P-450 isoenzymes. This activates the metabolism of both the drugs themselves and various compounds, including concomitant medications.

The mechanism of action of metadoxine is to activate enzyme systems that provide the processing of ethanol and acetaldehyde. In the process of metabolism, the drug breaks down into active metabolites – pyridoxine and pyrrolidone carboxylate. They increase the activity of alcohol dehydrogenase and acetaldehyde dehydrogenase, which accelerates the elimination of alcohol breakdown products. In addition, metadoxine increases the level of reduced glutathione, providing protection against oxidative stress. The effect on the cholinergic and GABAergic systems contributes to the reduction of neuropathological symptoms (Kvanchakhadze et al., 2025; Jiang et al., 2022).

Thioctic (alpha-lipoic) acid acts as a coenzyme in the processes of oxidative decarboxylation of pyruvic acid and alpha-keto acids. The mechanism of action of tiotriazoline is determined both by the presence of a thiol group in its structure, which possesses strong reducing and antioxidant properties (thiol groups act as scavengers of reactive oxygen species and free radicals; in mitochondrial dysfunction, thiol groups of the mitochondrial pore are oxidized, leading to mitochondrial dysfunction, energy deficit, and apoptosis), and by the ability of the molecule to activate compensatory pathways (malate–aspartate energy shuttle during ischemia, thereby reducing anaerobic glycolysis and lactate production) (Belenichev et al., 2025).

Tiotriazoline affects key links in the pathogenesis of diseases. Its main effects are:

1. Antioxidant effect – consists of several mechanisms: direct, by inactivating free oxygen radicals and reactive oxygen species; indirect, by reactivating antioxidant enzymes such as superoxide dismutase and glutathione peroxidase, and protecting endogenous antioxidants – α-tocopherol and glutathione – from depletion.

2. Anti-ischemic effect – enhances ATP synthesis and normalizes the respiratory chain.

3. Energotropic effect on mitochondria – increases the utilization of glucose, free fatty acids, and glycogen in cells, limits low-productive anaerobic glycolysis, prevents the development of lactic acidosis in cells, normalizes the activity of Krebs cycle enzymes, and under subtotal ischemia activates the compensatory malate–aspartate energy shuttle (more productive and safer than anaerobic glycolysis). A positive effect of tiotriazoline is that it activates the conversion of lactate to pyruvate.

4. Membrane-stabilizing effect – preserves the integrity of cell membranes, protects membrane phospholipids from lipid peroxidation, normalizes transmembrane processes, and maintains the threshold sensitivity of membrane receptors.

5. Anti-inflammatory and immunomodulatory effect – reduces circulating immune complexes, limits the release of inflammatory mediators by them, decreases the expression of the pro-inflammatory cytokine IL-1β, stabilizes the membranes of basophils, mast cells, and eosinophils, increases the phagocytic activity of macrophages, and raises interferon levels.

6. Reparative effect – stimulates epithelial regeneration, restores microcirculation, and activates protein-synthetic processes.

7. Anti-apoptotic effect – inhibits NO-dependent apoptosis mechanisms and increases the level of the anti-apoptotic protein Bcl-2.

Tiotriazoline demonstrates pronounced hepatoprotective properties in models of toxic, drug-induced, and alcoholic hepatitis, both when administered parenterally and orally, preventing mortality and clinical manifestations of the pathology. According to post-marketing studies, tiotriazoline contributes to the reduction of asthenic syndrome symptoms, improvement or almost complete normalization of cytolysis markers (ALT, AST) and cholestasis markers (γ-glutamyltransferase), and has a positive effect on blood lipid profile parameters in patients with non-alcoholic fatty liver disease (NAFLD) with liver fibrosis stages F0–F3.

In a pilot observational study (n = 80), tiotriazoline showed positive effects on clinical and biochemical activity indicators of NAFLD (including transaminase levels, fatty liver index (FLI)) and on the severity of cardiovascular risk predictors (total cholesterol,

LDL cholesterol, triglycerides, CRP). Parenteral administration of 100 mg/day for 5–10 days is considered appropriate, followed by oral tablets (300–600 mg/day) with a total course duration of at least 2 weeks (Samohalska, 2006).

In patients with chronic diffuse liver diseases of various etiologies (alcoholic, viral, mixed viral-alcoholic, non-alcoholic), the administration scheme with an initial parenteral dose of 100 mg/day was significantly more effective than 50 mg/day (Belenichev et al., 2019).

Alcoholic liver disease (ALD): in a randomized clinical trial, the addition of tiotriazoline to baseline therapy in patients with acute alcoholic hepatitis (n = 117) led to a faster decrease in alanine aminotransferase (ALT) activity, reduced total and indirect bilirubin levels, and increased overall treatment effectiveness based on clinical, biochemical, and instrumental assessments. Administration of the drug also positively influenced protein biosynthesis, restoring total protein and albumin levels in the blood of patients with ALD. Limited experience exists with the use of tiotriazoline in patients with liver cirrhosis (Child–Pugh class B).

Drug-induced liver injury: Tiotriazoline exhibited hepatoprotective effects in patients (n = 80) who received long-term antibacterial therapy, and also enhanced the effectiveness of a combination of silymarin and essential phospholipids in correcting hepatotoxicity induced by anti-tuberculosis drugs (n = 150).

Furthermore, tiotriazoline monotherapy reduced the severity of cytolysis syndrome in patients with non-Hodgkin lymphoma receiving chemotherapy protocols including doxorubicin, cyclophosphamide, vincristine, prednisolone, and rituximab (n = 150) (Mazur et al., 2025; Seminozhenko et al., 2025).

Selenium preparations (e.g., selenase) also demonstrate positive antioxidant properties. Their use has been proven in the treatment of pancreatitis and critical conditions. In addition, there is evidence of the effectiveness of selenium in the complex therapy of diseases of the cardiovascular and nervous systems (Mahfoz & Gawish, 2022).

The above sources have established the antioxidant and anti-inflammatory activity of herbal hepatoprotectors, and it has been determined that herbal preparations reduce the content of pro-oxidant cytokines and increase the activity of antioxidants (Xu et al., 2022; Mahfoz & Gawish, 2022; Sroor et al., 2022).

It is important that the simultaneous use of several drugs significantly increases the likelihood of drug-induced liver damage. When taking six or more drugs, the frequency of hepatotropic side effects reaches 80%. In the structure of morbidity, drug-induced liver damage ranks second after toxic hepatitis caused by ethyl alcohol, methyl alcohol, or alcohol substitutes.

Nearly half of all cases of acute liver failure are caused by drugs. The overall mortality rate for drug-induced liver injury remains high, ranging from 5% to 11.9% (Ray, 2022; Garcia-Cortes & Garcia-Garcia, 2022).

Liver diseases affect more than 10% of the world's population and are among the five most common causes of death in the world (Karlsen et al., 2022). The most common pathology is nonalcoholic fatty liver disease, which accounts for 40% of cases. Next in frequency among all hepatopathies are viral hepatitis B (30%), viral hepatitis C (15%) and alcoholic lesions (11%). Viral and alcoholic pathologies, drug damage, autoimmune hepatitis and primary biliary cirrhosis tend to progress. Over time, these conditions can progress to terminal stages, which is one of the main causes of mortality in world morbidity statistics (Muriel, 2017).

In recent years, the number of patients with liver fibrosis has increased (Zhao et al., 2024). Hepatoprotectors are administered for liver tumors (Batool et al., 2024). Herbal hepatoprotectors help with fatty liver disease (Moayyedkazemi et al., 2021). The complex herbal preparation "Liv52" protects the liver from severe damage (Kantharia et al., 2023).

The effectiveness of hepatoprotectors in liver cirrhosis and the possibility of an immunomodulatory effect have been established (Saeed et al., 2022). The effect of hepatoprotectors in phage conditions is associated with the activation of apoptosis (Ilukho et al., 2022).

The experiment showed the feasibility of including herbal hepatoprotectors in diabetes treatment regimens (Mahfoz & Gawish, 2022).

Herbal hepatoprotectors are added to drug therapy to reduce toxicity. They have similarly reduced the toxicity of acetaminophen (Pang et al., 2025). Herbal hepatoprotectors reduce the toxicity of the anti-tuberculosis drugs isonazid and refalicin (Anwer et al., 2023).

Hepatoprotective effect of plant extracts in the liver toxicity of paracetamol (Ilukho et al., 2022). In order to reduce the toxicity of the anticancer drug cisplatin, this drug is recommended to be taken with plant hepatoprotectors (Sherif, 2021).

Patients with chronic liver disease are at high risk of developing extrahepatic complications due to cirrhosis and portal hypertension. In addition, organ-specific disorders are observed, characteristic of certain nosologies. Such complications significantly worsen the quality of life of patients, and also increase morbidity and mortality rates both before and after organ transplantation (Goldberg & Fallon, 2015).

It has been proven that patients with cirrhosis of the liver have significantly more complicated bleeding, delayed tissue healing, and frequent ulcer recurrence compared to the general population. This creates an additional burden on the body and requires a comprehensive approach to therapy (Yang et al., 2021).

Today, there is a constant increase in the frequency of chemical hepatoses that occur due to the accumulation of various xenobiotics in the body. Hepatotoxic effects are caused by certain household chemicals, alcohol, industrial poisons – in particular chlorinated hydrocarbons and benzene derivatives, as well as certain drugs, such as paracetamol, nimesulide or isoniazid. In addition, poisonous plants and mushrooms, for example, pale toadstool (green fly agaric), are dangerous. Toxic substances can cause the development of hepatitis regardless of the route of their entry into the body through the respiratory tract, parenterally or digestive organs, since the liver is responsible for the metabolism of almost all foreign compounds. Depending on the concentration of toxins, massive death of liver cells can occur. This leads to the appearance of acute liver failure or the development of chronic intoxication with gradual degenerative changes. The latter option is especially dangerous in chronic viral hepatitis, when the body's compensatory capabilities are exhausted. With prolonged exposure to toxins, fatty degeneration most often occurs against the background of changes in connective tissue – nonspecific reactive hepatitis (Palmer et al., 2019).

According to the Anatomical Therapeutic Chemical Classification (ATC), hepatoprotectors belong to the section of drugs that regulate the digestive system and metabolic processes. They are allocated to a separate category of drugs for the treatment of liver and biliary tract pathologies under the code A05. The group of hepatotropic drugs includes such compounds as arginine glutamate, silymarin, cithiolone, epomediol, ornithine oxoglurate and arginine thidiazinc. This list also includes glycyrrhizic acid, metadoxine and phospholipids (Shepitko, 2019).

Alpha-lipoic acid, which previously belonged to this group, was transferred to another section due to its high importance in the treatment of complications of diabetes mellitus. Now it is classified as a substance that affects metabolic processes in general. A similar situation is observed with other known hepatoprotectors, which are located in different nodes of the ATS (Hofmann et al., 2021).

For example, the essential amino acid methionine is now considered an antidote, and its derivative ademetionine belongs to the group of amino acids that correct metabolism. Natural phospholipids in specific forms can also be found in the respiratory system section, where they are presented as pulmonary surfactants (Czigany & Tolba, 2022).

Global epidemiology demonstrates the seriousness of the problem of liver disease. According to available data, the prevalence of non-alcoholic fatty liver disease is the highest, affecting hundreds of millions of people. Projections for 2030 indicate further increases in the rates of most chronic pathologies, including steatohepatitis and alcoholic lesions (Repin et al., 2017).

Hepatoprotectors are mainly prescribed and continue to be used in complex therapy. On the one hand, they enhance the effects of other drugs, and on the other hand, they reduce the toxins of nonsteroidal, anti-inflammatory, analgesic, anti-tuberculosis drugs, antibiotics and antitumor drugs (Khan et al., 2024; Satyam et al., 2024; Tian et al., 2025; Halder et al., 2025).

Increased effectiveness of hepatoprotectors in the complex therapy of liver diseases has been established (Kukharchuk et al., 2025). The liver is one of the most important organs in the human body. It plays a fundamental role in the regulation of homeostasis and metabolic processes, including the metabolism of proteins, fats and carbohydrates. The organ also provides the deposition of iron and vitamins A, D, B12, participates in the metabolism of heme and bilirubin, detoxifies endogenous compounds and xenobiotics. Important functions of the liver include the synthesis and secretion of bile, the performance of immune tasks and the production of blood clotting factors.

According to WHO, over the past 20 years, there has been a clear trend in the world towards an increase in the number of liver diseases, which cause high mortality. According to the National Center for Health Statistics, the number of adults aged 18 and over with diagnosed liver pathology is 4.5 million people. This category of diseases ranks 10th in the overall mortality rating. Annual losses from cirrhosis, viral hepatitis and liver cancer account for about 4% of total mortality in the world, and every third death among women is associated with liver diseases (Hladkykh et al., 2023).

Hepatoprotectors include substances of different chemical structures, which are conventionally divided into six main categories. The first group consists of herbal preparations, such as legalon, silymar, carsil, rosilimar, hepabene, bienosilym, sibectan, phosphonciale, hepafor and artichol. The second category includes phospholipid preparations, which include essentiale, rezalyut, phosphogliv, esliver, phosphonciale, livolin, eslidin, vitrum eikonol and sikod. The third group is formed by amino acid derivatives, in particular L-ornithine-L-aspartate, glutamine-arginine, ademetionine and

methionine. The fourth group is represented by ursodeoxycholic acid preparations, such as grinderol, ukrliv, urosliv, ursofalk and ursochol. The fifth group includes selenium-containing drugs, such as Selenase, Livonorm, and Detoxil, and the sixth group includes drugs from other classes, including tocopherol acetate and ascorbic acid (Nagarajan, 2022).

According to the Anatomical Therapeutic Chemical Classification (ATC), these drugs belong to the group of drugs that affect the digestive system and metabolism (section A). They are intended for the treatment of liver and biliary tract diseases and have the code A05. The official name of the group is drugs used in liver diseases, lipotropic substances (A05B). The subgroup of hepatotropic drugs (A05BA) includes arginine glutamate (A05BA01), silymarin (A05BA03), epomediol (A05BA05), ornithine oxoglurate (A05BA06), thidiazinc arginine (A05BA07), glycyrrhizic acid (A05BA08), metadoxine (A05BA09) and phospholipids (A05BA10).

The purpose of combined use of hepatoprotectors can be to expand the spectrum of action or to unidirectionally enhance a certain effect due to synergism. An example of such an interaction is the combination of ademetionine and silymarin. Studies have confirmed that this combination suppresses inflammation and oxidative stress through two separate signaling pathways. Both substances inhibit the accumulation of fat in the liver, which has been demonstrated in clinical studies: in patients with metabolic-associated steatotic liver disease, a decrease in the degree of steatosis was observed according to ultrasound data (Patel et al., 2025).

The synergy of this combination is also manifested in the treatment of depressive states in steatotic liver disease and through the agonistic effect on the farnesoid receptor in alcoholic pathology. The effectiveness of such a combination in alcoholic hepatopathies has been clinically proven. In addition, the combination allows to expand the therapeutic coverage. Although both agents are effective in toxic lesions, there are specific situations for each of them. For example, silymarin is effective in poisoning with milk thistle, while ademetionine is indispensable in the treatment of intrahepatic cholestasis (Zhou et al., 2021)

Additional properties of silymarin, such as antifibrotic, immunomodulatory, choleretic and antiviral effects, significantly expand the possibilities of therapy. It is also involved in the regulation of apoptosis and stimulates hepatocyte regeneration. It is important that long-term administration of both ademetionine and silymarin contributes to an increase in the life expectancy of patients with liver cirrhosis. Thus, the combination of these substances (for example, in the drug "Adenomac Plus") is a pathogenetically justified and promising solution based on the principles of evidence-based medicine (Venugopal et al., 2024).

The effectiveness of combined hepatoprotective therapy directly depends on the logical pathogenetic justification for the feasibility of combining drugs. If such a basis exists, and the advantages of the combination are proven by research, this ensures high efficiency in real clinical practice. In the treatment of diseases of the hepatobiliary system, doctors often use several drugs simultaneously (Satyam, Bairy, Rehman, Attia, et al., 2024).

The joint use of hepatoprotectors is aimed either at expanding the spectrum of therapeutic action, or at unidirectional enhancement of a certain pharmacological effect through summation or potentiation. Today, there are a number of well-studied combinations, the clinical efficacy of which has been confirmed for specific nosological forms. In particular, the pharmaceutical industry produces fixed combinations, such as "Adenomac Plus", which have a clear pathogenetic justification for the simultaneous use of several hepatotropic components (Gubergrits et al., 2025).

The main focus is on the combination of S-adenosyl-L-methionine and silymarin (silybinin), since the drug "Adenomac Plus" is presented on the pharmaceutical market. It contains 500 mg of S-adenosyl-L-methionine and 210 mg of silymarin in each tablet. The rationale for this combination is based on the analysis of the summation of the effects of these two components. The transcription factors nuclear factor kappa (NF-kappa) and nuclear erythroid factor 2 (Nrf2) play a crucial role in modulating liver damage. Activation of NF-kappa triggers the production of pro-inflammatory molecules such as prostaglandin E2 (PGE2), interleukin-8 (IL-8) and macrophage chemotactic protein-1 (MCP-1). At the same time, Nrf2 is responsible for the regulation of genes that control antioxidant defense (Belenichev et al., 2025; Cui et al., 2026).

In experimental studies, it has been proven that the combination of ademetionine and silibinin reduces the production of PGE2, IL-8 and MCP-1, while blocking the transition of NF-kB into the cell nucleus. These processes are accompanied by an increase in the level of reduced glutathione. The combination of these substances inhibits inflammation and oxidative stress through two separate signaling pathways, which makes their joint use pathogenetically justified (Maksymenko et al., 2025).

The main mechanism of protection of ademetionine is its role as a methyl group donor in transmethylation processes. In addition, it exhibits a direct antioxidant

effect. Silymarin also acts as a powerful antioxidant. Its specific protective effect, especially in poisoning with the pale toadstool (Amanita phalloides), is to block the binding of toxins. Silibinin is incorporated into cell membranes, which physically prevents the penetration of the poison into hepatocytes. In the context of combination therapy, the summation of liver protection mechanisms when using ademetionine and silymarin (silibinin) is of key importance (Li et al., 2022).

In metabolic-associated steatosis of the liver (MASD), ademetionine is able to prevent or reduce the risk of developing fatty hepatosis. There are four main ways of excessive fat accumulation in the organ: increased intake of free fatty acids, decreased rate of their oxidation in mitochondria, increased synthesis of fatty acids, and impaired incorporation of triglycerides into very low density lipoproteins (VLDL). Ademetionine affects the pathogenesis of MASD as a precursor of glutathione and a donor of methyl groups for the synthesis of phosphatidylcholine. The latter is critically important for the formation of VLDL and the removal of triglycerides from liver cells. It has been experimentally proven that a deficiency of methionine and choline leads to a decrease in the level of ademetionine, fat accumulation, and the development of steatohepatitis. In studies on models lacking the MAT1A gene, which is responsible for the synthesis of ademetionine, lipid mobilization disorders were observed. Importantly, a decrease in the activity of this gene affects lipid formation even before visible changes appear in the tissues. The use of ademetionine for just seven days was sufficient to eliminate the deficiency of LDL and stabilize lipid metabolism (Bingül et al., 2024).

The expansion of the spectrum of therapeutic action of ademetionine and silymarin when used together is based on the unique properties of each component. The most important feature of ademetionine, which is not inherent in silymarin, is its participation in transsulfuration processes. Due to this, ademetionine shows high effectiveness in intrahepatic cholestasis, which accompanies various liver pathologies. This effect is confirmed by a number of high-proof studies (Fernández-Ramos et al., 2025).

Although both drugs are effective in toxic and medicinal lesions, there are significant differences in their use. Silymarin is a critically important emergency aid for poisoning with milk thistle. In European countries, its injectable forms are mandatory for intensive care units. A retrospective analysis of data from 2,000 patients over 20 years showed that the use of silymarin reduces mortality in mushroom poisoning to 5.8%, while without it this figure reaches 14.1%. Silymarin is also effective in acute toxic hepatitis caused by paracetamol overdose (Zane Horowitz, 2022; Jang et al., 2025).

In cases of chronic drug-induced hepatitis, the effectiveness of silymarin has been confirmed in the treatment of anti-tuberculosis and psychotropic drugs, as well as during chemotherapy of oncological diseases. Modern experiments also indicate its protective effect in lesions caused by D-galactosamine and lipopolysaccharides of gram-negative intestinal flora (Jafari et al., 2022).

Ademetionine is also successfully used to correct drug lesions during the therapy of tuberculosis and tumors. However, it is not included in the list of drugs for the treatment of poisoning with pale toadstool. Thus, the combination of these substances in the drug “Adenomak Plus” allows you to significantly expand the spectrum of therapeutic effects in various forms of toxic effects on the organ (Vincenzi et al., 2025).

The additional properties of silymarin are extremely important, which allow to significantly expand the spectrum of therapeutic effects of the combination. These include antifibrotic, antitumor, immunomodulatory and choleretic activity, as well as participation in the regulation of apoptosis and stimulation of hepatocyte regeneration. The antifibrotic effect of silymarin is due primarily to its ability to inhibit the transformation of hepatic stellate cells into myofibroblasts. This occurs by inhibiting fibrogenic pathways responsible for the formation of the cytoskeleton and collagen synthesis. Silymarin also exhibits antitumor effects that are associated with the control of oxidative stress, stimulation of apoptosis of damaged cells and regulation of the cell cycle. Studies on models of hepatocellular carcinoma have demonstrated its ability to affect different stages of carcinogenesis – from tumor initiation to progression (Omar et al., 2022; Venugopal et al., 2024).

The property of silymarin to promote organ regeneration is critically important for patients with chronic pathologies. This process is associated with the activation of ribosomal RNA synthesis, presumably through stimulation of the polymerase I enzyme, which accelerates the restoration of functional tissue. In particular, silymarin suppresses the matrix RNA of the growth factor TGF-beta, inhibits NF-kB and prevents the stimulation of stellate cells by regulating the production of extracellular matrix. Experimental data confirm that silymarin slows down the progression of early fibrosis and reduces the accumulation of collagen-1 in liver tissues (Venugopal et al., 2024).

Hepatoprotectors have a protective effect on all organs due to their effect on signaling systems (Gorchakova et al., 2025; Saleh et al., 2024). Ukrainian

scientists make a significant contribution to solving the issues of developing and implementing modern multicomponent hepatoprotectors (Volodina et al., 2017). The works of Ukrainian scientists are devoted to finding new mechanisms of action of hepatoprotectors (Golembiovska et al., 2019).

Conclusions. Thus, the data presented from domestic and foreign literature indicate the importance of searching for and studying hepatoprotectors. This group of drugs helps in everyday and military situations, because it relieves symptoms of digestive tract disorders. This group of drugs reduces or potentiates the effect of drugs prescribed for fibrosis, fatty liver disease, including carcinoma. The ability of hepatoprotectors to eliminate unpleasant and harmful symptoms when using necrotic analgesics (paracetamol), anti-steroidal, antitumor agents of various structures, and antibiotics is important. As a result, hepatoprotectors, especially of plant origin, are low-toxic, effective drugs that need to be further investigated in preclinical and clinical conditions due to their effectiveness and safety.

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